Tear Function Parameters Before and After Corneal Collagen Crosslinking

Prof. Dr. Osama El Said Shalaby, Assist. Prof. Dr. Amr Mahmoud Awara, Dr. Molham Abd El Hafez El Bakary, and Heba Allah Abd El-Monsef Ibrahim Agha (M.B.B.CH)

Ophthalmology Department, Faculty of Medicine, Tanta University, Egypt
drheba59@yahoo.com

Abstract: Purpose: To evaluate tear function parameters before and after corneal collagen cross-linking. **Methods**: prospective interventional randomized uncontrolled longitudinal study included 40 eyes of 30 patients with average age 23.8±5 who were prepared for CXL. The patients were divided into 2 groups: Group 1 had CXL without removal of the epithelium. Group 2 with removal of the epithelium. each group was further subdivided into 2 subgroup accelerated and standard techniques. The tear film was evaluated by measuring lower tear meniscus height (TMH), break up time (BUT), schirmer test and staining with fluoresce in, rose bengal and lissmain green stains. **Results**: TMH in post operative 1st week visit showed slight difference between epi on and off. there was no significant difference between both techniques in both groups. A minimally significant difference in Schirmer test was noted in the 1stand week post operative between epi on and off techniques. no difference preoperative and in the other follow up visits. BUT values were nearly straight forward the whole way of the follow up. There was no staining pre or post operative. **Conclusion**: there is no significant changes in the tear function parameters after CXL.
[Osama El Said Shalaby, Dr. Amr Mahmoud Awara, Dr. Molham Abd El Hafez El Bakary, and Heba Allah Abd El-Monsef Ibrahim Agha. **Tear Function Parameters Before and After Corneal Collagen Crosslinking.** *Nat Sci* 2018;16(8):1-7]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). http://www.sciencepub.net/nature. 1. doi:10.7537/marsnsj160818.01.

Key Words: tear function parameters – corneal collagen crosslinking

1. Introduction

The preocular tear film plays an important role in overall ocular health and function. It is approximately 7micron thick and comprises lipid, aqueous and mucin layers. The outermost lipid layer is produced by the meibomian glands and serves to stabilize the tear film and slow evaporative losses. The middle aqueous layer constitutes 90% of the tear film thickness and is produced by the lacrimal gland. The innermost layer comprises mucins produced by conjunctival goblet cells and membrane-associated mucins produced by epithelial cells. (1,2)

Dry eye disease (DED) is an immune inflammatory disorder of the tear film and ocular surface and is one of the most common ophthalmic conditions for which patients present to healthcare providers. It is characterized by symptoms of dryness, visual instability, foreign body sensation and irritation, all of which have a significant negative impact on patient quality of life. Although the mechanisms underlying DED continue to be investigated, there is evidence to suggest that dysfunction of both the innate and adaptive immune responses contribute to DED pathophysiology. (2)

Keratoconus is the most common primary ectasia. It is a bilateral and asymmetric corneal degeneration characterized by localized corneal thinning which leads to protrusion of the thinned cornea. Corneal thinning normally occurs in the inferior temporal as well as the central cornea, although superior localizations have also been described. Corneal protrusion causes high myopia and irregular astigmatism, affecting visual quality. It usually becomes apparent during the second decade of the life, normally during puberty, although the disease has also been found to develop earlier and later in life, and it typically progresses until the fourth decade of life, when it usually stabilizes. A recent study has determined that 50% of non-affected eyes of subjects with unilateral keratoconus will develop the disease in 16 years. (3)

CXL with riboflavin and UVA is a new technique of corneal tissue strengthening that combines the use of riboflavin and UVA irradiation. Riboflavin works as a photo sensitizer for the induction of crosslinks between collagen fibrils and at the same time act as a shield from the penetration of UVA in the underlying tissues (4)

As a treatment modality for keratoconus, CXL was introduced. As a procedure performed on the eye, CXL effect on the tear film was studied severally to find out any changes that may be introduced to the tear film as a result of the procedure

Aim of The Work

Evaluation of the tear function parameters before and after Corneal Collagen Cross-linking (CXL) in eyes with keratoconus.

Study design*:*

Prospective interventional randomized uncontrolled longitudinal study.

2. Patients and Methods

This is a prospective interventional randomized uncontrolled longitudinal study that was conducted on 40 eyes of 20 patients who visited the cornea clinic of Tanta University and Tanta Ophthalmology hospitals.

Inclusion criteria:

Patients proved to have keratoconus and scheduled for CXL.

Exclusion Criteria:

1- Patients with systemic diseases causing dry eye e.g rheumatoid patients.

2- Patients with other corneal or ocular pathology e.g corneal degeneration, scaring.

3- Any history of ocular surgery e.g refractive surgery.

All included patients were submitted to the following:

1-Complete ophthalmological evaluation:

History:

1- Personal history including age, sex and occupation.

2- History of the present illness for symptoms of dry eye like burning sensation, lacrimation, blurring.

3- History of systemic illness e.g rheumatoid arthritis or drug intake e.g antihistamines for allergy and beta blockers for heart problems.

4- Past history of previous ocular surgery, trauma or previous CXL.

5- Family history of similar condition.

Examination:

1- Patient refraction and best corrected visual acuity were assessed.

2- K readings (K1 and K2) and corneal thickness (central and thinnest location were recorded.

3- External appearance for any gross abnormality e.g. proptosis and facial palsy, entropin or ectropion.

4- Detailed bimicroscopic slit lamp examination:

- Cornea for signs of keratoconus which was minimal or absent in mild cases and included: Enhanced appearance of the corneal nerves, Vogt striae (fine-stress lines) in the deep stroma, iron deposits in the basal epithelial cells in a (often partial) ring shape at the base of the conical protrusion called the Fleischer ring, Munson sign.
- Ocular surface for signs of dry eye including redness, foamy discharge at the medial and lateral canthi and bitot spots.

Special tests:

Lower tear film meniscus height measurement:

The height was measured roughly by the slit lamp with narrow straight vertical beam set at 1mm. The tear meniscus height was measured from lid margin to the top of the meniscus. Gentle vertical manipulation of the lower lid with a finger was helpful to detect the top of the meniscus. ≥1mm was considered normal <1mm decreased tear production.

Schirmer test:

White what man filter paper (35 ×5 mm) strips were folded 5mm from one end and placed into inferior fornix at the junction of the medial two thirds and the lateral one third of the lower eye lid. After 5 minutes, the amount of wetting was measured. Normal wetting was greater than 15 mm.

- 10- 15mm suspicious
- 5-10mm moderate dry eye
- <5mm severe dry eye

Tear break up time:

One drop of sodium fluorescein 2% was instilled into the tear film and, The patient was asked to blink then to stop blinking and observing the pre corneal tear film then count the time from the first appearance of dry spot. Break-up occurs most frequently in the inferior or central cornea.

- 10 seconds is average
- 5-10 marginal dryness
- Less than 5 indicative for dryness

Staining of the cornea and conjunctiva:

Fluorescein staining:

A fluorescein impregnated paper strip (wetted with a drop of saline) was inserted in the lower conjunctival fornix and the eye then was visualized using the cobalt blue filter of the slit lamp.

Rose Bengal staining:

Rose bengal impregnated paper strip was inserted in the lower conjunctival fornix after application of topical anesthesia (Benox (Benoxinate hydrochloride) 4% E.I.P.I.CO.10th Ramadan City. Industrial Area. Egypt) and the eye was examined for any tissue staining.

Lissamine green staining:

Lissamine green impregnated paper strip (wetted with a drop of saline) was inserted in the lower conjunctival fornix to stain the devitalized tissue like rose bengal but was less irritant.

Grading was performed 1-4 minutes after staining.

Scoring system:

Van Bijsterveld system was available to grade the ocular surface staining. It divides the ocular surface into 3 zones: nasal bulbar conjunctiva, temporal bulbar conjunctiva and cornea. Each zone is evaluated on a scale of 0-3, with 0 indicating no staining and 3 indicating confluent staining. The maximum possible score with this system is 9. [5]

	Grade 0	Grade 1	Grade 2	Grade 3
staining	0	1-3	4-6	7-9

The patients were divided into 2 groups as the following:

Group 1: included 20 eye with epi- on technique.

The cornea was allowed to keep its epithelium while performing the procedure.

They were divided into 2 subgroups:

Group 1-a: 10 eyes with accelerated technique of CXL.

Accelerated 45 mW/cm2 CXL protocol with pulsed technique (1 second on and 1 off) and total time of exposure 5.20 minutes with energy 7.2 J/cm2). Paracel (Riboflavin, 25% Benzalkonium chloride, EDTA, Trometamol, Hydroxy propyl methylcellulose, phosphate buffered saline solution) and Vibex Xtra (Riboflavin 0.22% phosphate buffered saline solution) are used for 11 minutes soaking the cornea before UVA exposure as the following:

Paracel is used at 0 m, 1.5m,3m,4.5m then washing the cornea with vibexxtra 4 drops and then used drop by drop at 6.5m, 8m, 9.5m,11m. The cornea then is exposed to UVA using **Avedro KXL crosslinking system** (Waltham, Mass, USA). During exposure BSS (Blanced Salt Solution) is used every 2 minutes. At the end cornea was washed with BSS and an eye bandage was applied.

Group 1-b: 10 eyes with standard technique of cxl:

"Standard" 3 mW/cm2 CXL protocol (standard CXL 3 mW) receiving riboflavin 0.25% eyedrops every 5 minutes for 30 minutes before exposure of the central 9.0 mm region of the cornea to UVA light with a fluency of 3 mW/cm2 for 30 minutes using **CSO VEGA CBM-X-Linker** (SCANDICCI (FIRENZE)-Italy). Riboflavin eye drops were reapplied at 5 minute intervals throughout the period of irradiation.)109) (Figure (19).

Group 2:

Included 20 patients with epi off technique. Epithelial debridement was done before going through the main steps of the procedure by applying Topical anesthesia (Benox) and alcohol for 2min. With an 8 mm diameter trephine blade, the central mark is placed over the epithelium.

Mechanical epithelial debridement of the previously marked central 8 mm of the cornea was carried out gently using a sponge without disturbing the sub epithelial components. This was to ensure that the riboflavin penetrates the stroma in order to achieve a high level of UVA absorption.

They were divided into 2 subgroups.

Group 2-a:

10 eyes underwent the accelerated technique of CXL after epithelial removal. Vibex rapid (.0.1 Riboflavin, Hydroxypropylemethyle cellulose) was dropped 1 drop over the cornea every 2 m for 10 m then exposed to UVA (power 30 mw/cm2, pulsed technique of exposure 4 m with total time 8 m and energy 7.2J/cm2) using **Avedro KXL crosslinking system** (Waltham, Mass, USA). Contact lens was applied over the operated cornea.

Group 2-b:

10 eyes with standard technique of CXL after epithelial removal. "Standard" 3 mW/cm2 CXL protocol (standard CXL 3 mW) receiving riboflavin 0.1% eyedrops in 20% dextran T-500 every 5 minutes for 30 minutes before exposure of the central 8.0 mm region of the cornea to UVA light with a fluence of 3 mW/cm2 for 30 minutes using CSO VEGA CBM-X-Linker (SCANDICCI (FIRENZE)-Italy). Riboflavin eyedrops were reapplied at 5 minute intervals throughout the period of irradiation.)109)

Post operative treatment:

Patients received combined topical (antibiotic/ steroid, dexamethasone/ tobramycin) (tobradex®Alcon Fortworth, Texas, U.S.A) eye drops, was used 5 times per day and lubricant (carboxymethylecellulose sodium 0.5% (Refresh tears ® Allergan Waco, Texas, U.S.A) 5 times as well. Contact lens were applied to epi off operated eyes.

Post operative follow up:

The patients were examined one day, one week for redness, irritation and healing. Two weeks, one month, two months and three monthespost operative, evaluation of the tear film measuring tear function parameters including lower tear meniscus height, Schirmer test, BUT and ocular surface staining with fluorescein, rose bengal and lissamine green stains was done. Contact lens was removed in the 1st weak visit.

3. Results

Table (1) Age distribution of the patients

	EPI						T-Test	
	On			**Off**				
	Mean	**±**	**SD**	**Mean**	**±**	**SD**	**t**	**P-value**
Age	23.800	±	5.177	21.150	±	3.843	1.300	0.210

Statistical analysis:

Data was analyzed using SPSS (Statistical Package for Social Sciences) v20.0 (SPSS Inc., Chicago, USA). Qualitative data was presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data was

presented as mean ± SD. Student t-test was used to compare between two groups.

This study included 40 eyes of 20 patients underwent CXL for keratoconus. 20 eye with epi- on technique (50%) and 20 eyes with epi-off (50 %). Group (1) with epi-on technique had 10 eyes operated with accelerated technique and 10 eyes with the standard one. The same was for group (2).

Demographic data:

Table (2) Sex distribution

Sex	EPI						Chi-Square	
	On		**Off**		**Total**			
	N	**%**	**N**	**%**	**N**	**%**	**X^2**	**P-value**
Female	5	50.00	4	40.00	9	45.00	0.000	1.000
Male	5	50.00	6	60.00	11	55.00		
Total	10	100.00	10	100.00	20	100.00		

Table (3) Schirmer in epion accelerated and standard techniques

EPI On Schirmer	Tech						T-Test	
	Accelerated			**Standard**				
	Mean	**±**	**SD**	**Mean**	**±**	**SD**	**t**	**P-value**
Pre	16.600	±	0.966	17.400	±	6.041	-0.414	0.684
Post 2 Weeks	15.600	±	1.174	15.600	±	5.317	0.000	1.000
Post 1 Month	16.100	±	1.197	16.500	±	6.151	-0.202	0.842
Post 2 Months	16.400	±	1.075	17.400	±	6.501	-0.480	0.637
Post 3 Months	16.600	±	0.966	17.400	±	6.501	-0.385	0.705

In epi off standard and accelerated techniques, there was minimal significant difference only in the 2nd week (p value =,0.005). (table (11) figure (27)

Table (4) Schirmer in epi off accelerated and standard techniques.

EPI Off schimer	Tech						T-Test	
	Accelerated			**Standard**				
	Mean	**±**	**SD**	**Mean**	**±**	**SD**	**t**	**P-value**
Pre	16.100	±	0.994	16.400	±	1.430	-0.545	0.593
Post 2 Weeks	14.500	±	1.179	12.000	±	2.160	3.213	0.005*
Post 1 Month	16.200	±	0.919	14.500	±	2.550	1.984	0.063
Post 2 Months	16.200	±	0.919	15.400	±	3.098	0.783	0.444
Post 3 Months	16.200	±	0.919	15.400	±	3.098	0.783	0.444

A slight significant difference in schirmer test was noted in the 2nd week postoperative between epi on and off techniques. no difference preoperative and in the other follow up visits. (p value =0.019)

In epi on procedure, there was no statistical difference between standard and accelerated techniques effect on the lower tear meniscus height pre and post operative. (P value in 2nd week =0.136)

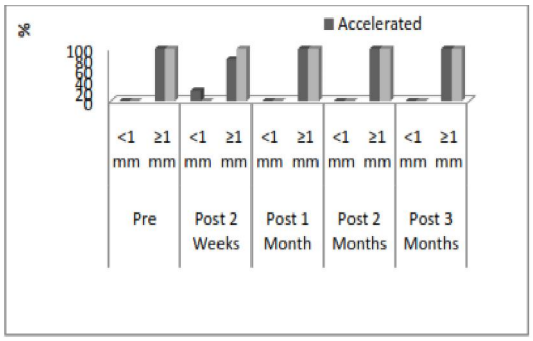

Figure (1) Lower tear meniscus height in epi on accelerated and standard techniques

In epi off procedure, there was no statistical difference between standard and accelerated techniques effect on the lower tear meniscus height pre and post operative. (P value in 2nd week =0.606)

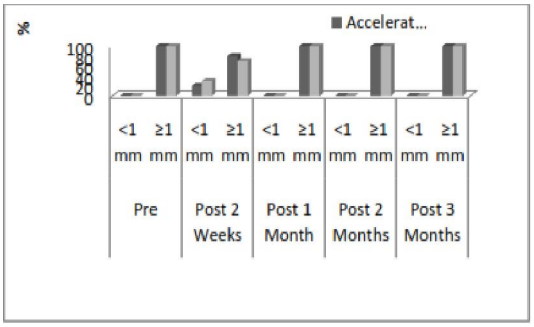

Figure (2) Lower tear meniscus height n epi off accelerated and standard techniques

In preoperative evaluation of Lower tear meniscus height there was no statistical difference between epi on and off techniques. In the follow up visits post operative, we also didn't find any statistical difference (p value=.0.212 in the 2nd week visit.

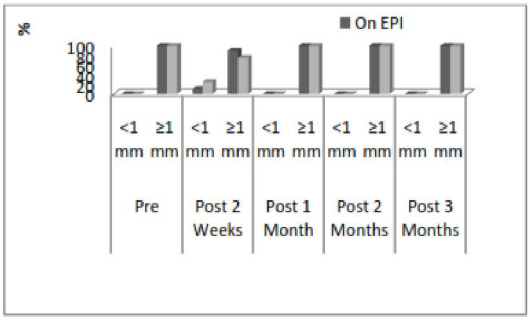

Figure (3) Lower tear meniscus height evaluation in epi on and off

No statistical difference values between accelerated and standard techniques were found in Schrimer test in epi on eyes.

Comparing accelerated and standard techniques effect on BUT in epi on eyes, there was no statistical difference effect pre and post operative. The same comparison when held on epi off accelerated and standard techniques revealed no statistical difference as well. Also there was no significant changes in the follow up visits.

Table (5) Schirmer in epi on and off

Schirmer	EPI						T-Test	
	On			**Off**				
	Mean	**±**	**SD**	**Mean**	**±**	**SD**	**t**	**P-value**
Pre	17.000	±	4.230	16.250	±	1.209	0.762	0.451
Post 2 Weeks	15.600	±	3.747	13.250	±	2.124	2.440	0.019*
Post 1 Month	16.300	±	4.318	15.350	±	2.059	0.888	0.380
Post 2 Months	16.900	±	4.564	15.800	±	2.262	0.966	0.340
Post 3 Months	17.000	±	4.542	15.800	±	2.262	1.058	0.297

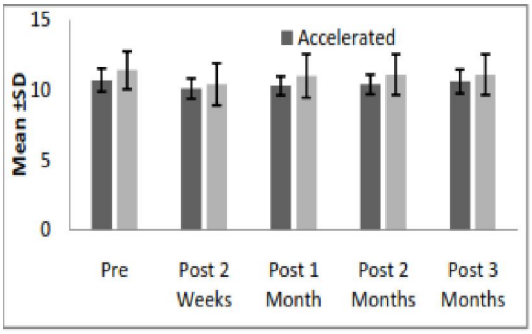

Figure (4) BUT in epion accelerated and standard techniques

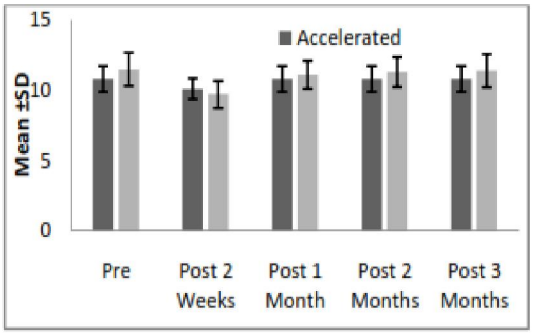

Figure (5) BUT in epi off on accelerated and standard techniques

BUT between epi on and off techniques showed no statistical difference pre and post operative

Table (6) BUT in epi on and off

BUT	EPI						T-Test	
	On			Off				
	Mean	±	SD	Mean	±	SD	t	P-value
Pre	11.050	±	1.146	11.150	±	1.089	-0.283	0.779
Post 2 Weeks	10.250	±	1.164	9.900	±	0.852	1.085	0.285
Post 1 Month	10.650	±	1.226	10.950	±	0.945	-0.867	0.391
Post 2 Months	10.750	±	1.164	11.050	±	0.999	-0.875	0.387
Post 3 Months	10.850	±	1.182	11.100	±	1.071	-0.701	0.488

Regarding staining of the eyes with fluorescein, rose bengal and lissamine green stains, no eyes were stained preoperative or post operative. They took grade 0 with the scoring system.

4. Discussion

Tear film covering ocular surface has a protective, visual and defensive functions of the eye that's why it is important to study the effect of any

manipulation or interference that may cause any changes in its structure and function.

Many studies have been conducted to evaluate the effect of CXL on tear film structure and function as it is considered the first line defense in front of the uvradiation. it was important to detect any harmful effects induced by the rays that may alter tears composition and affect its function. This research on the CXL epithelium-on technique did this study was of considerable duration (12 months) and took into account most factors considered important for evaluation of the eye surface. No significant changes from baseline were noted for any of the parameters studied. This allows us to conclude that CXL, at least in its accelerated form with pulsed light, does not likely affect the tear function either in the medium term or in the long term. [6]

There was no significant change in a study that evaluated the parameters of dry eye including only Fl and RB staining, tear film meniscus height, and TBUT values after standard CXL. Performing additional tests to evaluate the ocular surface and tear functions can provide more data options for dry eye disease as they also pointed out in this study. [7]

Other results showed minimal differences (not statistically significant), in the long-term evalution of the studied parameters. However, there were some partial differences for specific parameters at different time points. The Ocular Surface Disease Index showed differences between baseline and at 3 and 6 months, although they were not statistically significant (P = 0.083 and 0.086, respectively). Likewise, the Schirmer demonstrated some differences at 3 months (P = 0.063), but not later. It has been reported that keratocytes and the sub epithelial nerve plexus regenerate after 6 months. [6]

Several research groups have studied some of the parameters analyzed. None of these authors found statistically significant differences in the medium or long term for any of the parameters assessed. [7,8,9] Only Kalkan Akçay et al [8] have found alterations in the conjunctival impression cytology at 3 months and ascribed them to the toxicity of UVA radiation. The changes observed in that study, such as loss of goblet cells and possible changes in mucin secretion, did not translate into TBUT disorders. The SCH results were not altered according to their study. Interestingly, other authors have found that TBUT in patients with keratoconus is reduced; this has been attributed to decreased levels of goblet cells in these patients. [10] Such baseline differences in comparison with normal subjects might affect the postoperative course.

Reduced sensitivity after CXL in patients with low tear break-up time theoretically could generate dry eye–related problems because of the decreased blinking rate and increased tear evaporation and exposure of corneal epithelium surface. The results of this study demonstrate that because TFBUT and Schirmer's I test results were not affected, dry eye does not seem to be a significant complication of CXL in patients with keratoconus. [9]

In a current study, the results demonstrated that basic tear secretion And TFBUT are not affected by CXL. The patients included in the study were advised to use preservative-free artificial tears, which may have helped. On the other hand, the sensitivity of the peripheral un affected part of the cornea may be sufficient to regulate basic tear secretion or the aberrant activity of the amputated corneal nerves may contribute to this. [11]

Examining the impact of CXL on the ocular surface by vital staining, this study did not reveal a statistically significant effect after 3 and 6 months. the findings suggest that potential limbal stem cell injury during the CXL procedure has no significant effect resulting in postoperative dry eye. Additionally, potential damage to corneal nerves during the CXL procedure does not appear to affect the surface lubrication a Pathologic staining with fluorescein was evident in 1 eye before CXL, 1 eye of a different patient 3 months postoperatively, and 1 eye of a third patient 6 months postoperatively). Differences between visits were not statistically significant (*P* =.607).

Rose bengal staining at 3 and 6 months was comparable to preoperative staining. Differences between visits were not statistically significant (*P*=.590).

Tear film height was reduced in more eyes 3 months postoperatively than before CXL. Tear fi lm height was normal in all eyes 6 months postoperative. Differences between visits were not statistically significant (*P* =.135). The number of eyes with reduced tear fi lm break-up time (< 10 sec) was not significantly changed 3 and 6 months postoperatively (*P* =.247) after 3 months. [7]

In our study, it was noted that there was no significant difference regarding age and sex. The mean value of K1 readings was 45.3 D with range from minimum to maximum 41.6-55.4 D. The mean value of K2 was 48.865 D with range from 43.3-59.5D. preoperative evaluation of tear film revealed no dryness. Regarding epi on and off technique in general there was no significant difference in lower tear meniscus height (p value=.0.212 in the 2nd week), Schirmer test at the 2nd week showed minimal significant difference (p value =0.019). No significant changes in the BUT preoperative and in the whole follow up period.

Regarding accelerated and standard techniques there was no significant changes in epi on (TMH p value in the 2nd week= 0.136. Schirmer and BUT

showed no significant changes). Epi-off (TMH p value in the 2nd week=0.267, Schirmer showed slight significant change in the 2 weeks' visit. (p value=0.005), BUT results revealed no significant changes).

There was no staining neither preoperative nor postoperative with fluorescein, rose bengal or lissamine green stains. The scoring system for staining was zero.

Conclusion

CXL doesn't permanently modify tear function parameters after 3 months follow up regarding Schirmer, BUT, lower tear meniscus height and staining with fluorescein, rose bengal and lissmaine green. CXL is safe and has no effect on tear film either with epi on or off, accelerated or standard techniques.

Recommendations

CXL is still recommended as an effective treatment modality in management of keratoconus. Tear function evaluation is important to be considered before and after this procedure.

According to our study results, there are no serious hazards on the tear film after cxl as there are no permanent changes in tear constituents or obvious effect on tear film stability. The tear film is very well functioning after the procedure that is why it is allowed to do cxl for eyes with keratoconus without any worries regarding tear film.

Further studies could be conducted on larger scale including more parameters for longer period of follow up.

References

1. Leyngold IM, Chuck RS. Corneal Surgery. Brightbill FS, editor. Amsterdam, The Netherlands: Mosby Elsevier; 2009. pp. 17–23.; Ch. 3.
2. Dohlman T, Ciralsky J, Lai E: Tear film assessments for the diagnosis of dry eye. Current Opinion in Allergy and Clinical Immunolog 2016;16:487-491.
3. Romero-Jimenez M, Santodomingo-Rubido J, Wolffsohn J. Contact Lens and Anterior Eye 2010;33:157-166.
4. Iseli HP, Thiel MA, Hafezi F, et al. Ultraviolet A/riboflavin corneal cross-linking for infectious keratitis associated with corneal melts. cornea 2008;27(5):590-594.
5. Savini G, Prabhawasat P, Kojima T, et al: The challenge of dry eye diagnosis. Clinical ophthalmology (Auckland, N. Z)2008;2:31-55.
6. José I. Recalde, Arantxa Acera et al. Ocular Surface Disease Parameters After Collagen Cross-Linking for Keratoconus 2016. Wolters Kluwer Health.
7. Taneri S, Oehler S, Asimellis G, et al. Influence of corneal cross-linking keratoconus on several objective parameters of dry eye. J Refract Surgfor 2013;29:612–616.
8. Kalkan Akçay E, Kilicarslan A, Uysal BC, et al: Tear Function and Ocular Surface Alterations After Accelerated Corneal Collagen Cross-Linking in Progressive Keratoconus. Eye and Contact Lens 2016 p. 203.
9. Kontadakis GA, Kymionis GD, Kankariya VP, et al. Effect of corneal collagen cross-linking on corneal innervation, corneal sensitivity and tear function of patients with keratoconus. Ophthalmology. 2013;120: 917–922.
10. Dogru M, Karakaya H, Ozçetin H, et al. Tear function and ocular surface changes in keratoconus. Ophthalmology. 2003;110:1110–1118.
11. Belmonte C. Eye dryness sensations after refractive surgery: impaired tear secretion or “phantom” cornea? J Refract Surg 2007;23:598–60.

6/6/2018